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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/621,468	07/24/2000	Lee Arnold	BBI-6049	4509
959	7590	04/12/2004	EXAMINER KIFLE, BRUCK	
LAHIVE & COCKFIELD, LLP. 28 STATE STREET BOSTON, MA 02109			ART UNIT 1624	PAPER NUMBER

DATE MAILED: 04/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/621,468	ARNOLD ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Bruck Kifle, Ph.D.	1624	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 13 February 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 18-21, 23-28 and 30-45 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 18-21, 23-28 and 30-45 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/13/04 has been entered.

Applicant's amendments and remarks filed 2/13/04 have been received and reviewed. Claims 18-21, 23-28 and 30-45 are pending in this application. Applicants should note that claims 1-17 and 22 are not present in this application and their listing in the claims is incorrect. See amendments filed 06/06/02. Also, Applicants cannot withdraw claim 40. The claim is still pending. Is cancellation intended? Appropriate correction of the listing of claims is required.

Note that compounds, corresponding compositions, a method of use and a process of making that are of the **same** scope are considered to form a single inventive concept. Claims 18 and 28-39 are now of different scopes. Applicants should either amend these claims so they are of the same scope or elect a group to be examined. Should Applicants maintain different scopes in response to this office action, a written restriction requirement will be made. The method claims are now being examined to the extent that they reflect the compound claim in scope.

***Claim Rejections - 35 USC § 112***

Claim 18 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Provisos have been included in these claims that (i) excludes 12 species and

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(ii) reads "provided that when R<sup>1</sup> is methyl, R is not hydroxymethyl, nitrophenyl, m-OCH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>, 4-hydroxy-3-methoxyphenyl or 2-hydroxy-3-bromophenyl." These provisos lack description.

The basis of this rejection is the same as given in the previous office action and is incorporated herein fully by reference.

Negative limitations require a description. The specific compounds were previously not disclosed and the new concept that has been introduced by the proviso is the specific relationships between the variables R<sup>1</sup> and R. This specific relationship of connectivity was previously not disclosed. This notion that the definition of one variable depends on the definitions of other variables is new. The definition of a variable is no longer independent.

Regarding the method of claims 28-36, where it was deemed that these claims would read on inhibiting one or more protein kinase activities *in vitro*, inhibiting one or more protein kinase activities in mammals with below normal protein kinase activities, inhibiting one or more protein kinase activities in mammals with normal protein kinase activities, or in asymptomatic mammals with up-regulated protein kinase activities and that the specification fails to teach any benefit to be gained from such actions, Applicants argue that the instant compounds can be subjected to assays to test for inhibition of protein kinase activity. Self-study of a compound is not a patentable utility. An example would be to burn a compound to see how much energy it has or to run a compound through HPLC to study the retention time of the inventive compound.

Regarding the second prong of this rejection, Applicants arguments have been fully considered but are not persuasive. Claim 28 is drawn to inhibiting one or more protein kinase activities selected from 16 kinases but one skilled in the art would not know how to use these

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compounds. The how to use portion of the statute has still not been addressed. This means that Applicants must teach the skilled practitioner, in this case a physician, how to treat a given subject. The physician clearly must know what disease and what symptoms are to be treated. In a case concerning the patentability of compounds with "good effects against a wide range of insects" *In re LORENZ AND WEGLER*, 134 USPQ 312 U.S. Court of Customs and Patent Appeals upheld the rejection of compound claims, noting that "[a]ppellants are seeking a seventeen year monopoly. We would remind them that if they have in truth invented something which promotes the progress of science and the useful arts, then in exchange for a patent grant they must make a full and complete disclosure of their invention, leaving nothing to speculation or doubt. That Congress so intended is evident from the strong and comprehensive language of Section 112 which appellants here have failed to satisfy." In this case, Applicants have not provided what is being treated by claim 28, who the subject is, how one can identify said subject (i.e. how one can identify a subject in need), given no specific dose, given no specific dosing regimen, given no specific route of administration, and do not specify what diseases or symptom they intend to treat.

In a case, *In re MOUREU AND CHOVIN*, 145 USPQ 452, concerning the patentability of antitubercular compounds, The U.S. Court of Customs and Patent Appeals held "[i]t is therefore clear that those skilled in the art who desire to use the products of the invention for medicinal purposes would find it necessary to engage in extensive experimentation to determine what would be the effective and safe manner of using the products as medicines for the suggested purposes and to determine the dosages to be avoided because lethal or ineffective. Both the examiner and the board recognized that compliance with section 112 does not necessarily require

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specific recitations of use if the method of using is inherent in the description of the compound, *In re Nelson*, 47 CCPA 1031, 280 F.2d 172, 126 USPQ 242. The board held, however, that a bald assertion that the claimed compounds possess antitubercular activity would not indicate to those skilled in the medical arts the manner of effectively using the compounds.”

As the Supreme Court said in *Brenner v. Manson*, 148 USPQ at 696: “a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.” As U.S. Court of Customs and Patent Appeals stated *In re Diedrich* 138 USPQ at 130, quoting with approval from the decision of the board: “We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.”

Claims 37 and 38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicant's arguments have been fully considered but is not persuasive. The basis of this rejection is the same as given in the previous office actions and is incorporated herein fully by reference. The ability to treat any and all of the diseases recited in these claims is *prima facie*

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not enabled. The diseases recited It has been recited in claim 10, a method of treating neurodegenerative disorders. There is no such agent that can treat any and all of the diseases because the disorders are extremely varied in origin and nature of effect. The origin and the nature of the diseases are different one from the other. The symptoms and nature of these diseases are also different one from the other.

Claim 18-21, 23-28 and 30-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the definitions of  $R^3$ ,  $R^4$  and  $R^5$  the phrase "lower alkyl ester" is present. This, however, is not a radical but a compound. An ester is a compound with no open valency. Appropriate correction is required.

***Claim Rejections - 35 USC § 102***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim 18 is rejected under 35 U.S.C. 102(b) as being anticipated by Barnikow et al. (Chemische Berichte (1967), 100(5), 1661-6. The reference teaches the compound with RN 16105-53-6 which corresponds to the compound of the instant claim when in the instant case  $R^1$  is -OiPr and R is nitrophenyl (see CAS abstract).

Claim 18 is rejected under 35 U.S.C. 102(b) as being anticipated by Misawa et al. (JP 52051366). The reference teaches the compound with RN 63554-75-6 which corresponds to the compound of the instant claim when in the instant case  $R^1$  and R are both phenyl groups (see CAS abstract).

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Claim 18 is rejected under 35 U.S.C. 102(b) as being anticipated by Ege et al. (Journal of the chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1983), (2), 325-31). The reference teaches the compound with RN 85921-36-4 which corresponds to the compound of the instant claim when in the instant case  $R^1$  is hydrogen and R is methoxyphenyl (see CAS abstract).

Claim 18 is rejected under 35 U.S.C. 102(b) as being anticipated by Schmidt et al. (Journal of Organic Chemistry (1983), 48(23), 4367-70). The reference teaches the compounds of RN 87192-00-5, 87192-01-6, 87192-02-7, 87192-03-8 and 87192-04-961-14-6 which corresponds to the compound of the instant claim when in the instant case  $R^1$  is hydroxymethyl and R represents trimethoxyphenyl, chlorophenyl, phenyl and nitrophenyl (see CAS abstract).

Claim 18 is rejected under 35 U.S.C. 102(b) as being anticipated by Imai et al. (JP 62029570). The reference teaches the compound with RN 108402-26-2 which corresponds to the compound of the instant claim when in the instant case  $R^1$  is methyl and R is 4-hydroxy-3,5-bisisopropyl phenyl (see CAS abstract).

Claim 18 is rejected under 35 U.S.C. 102(b) as being anticipated by Dubau et al. (Chemische Berichte (1983), 116(7), 2714-16). The reference teaches the compound with RN 87161-14-6 which corresponds to the compound of the instant claim when in the instant case  $R^1$  is hydroxy and R is dimethylamino phenyl (see CAS abstract).

Claim 18 is rejected under 35 U.S.C. 102(b) as being anticipated by Mitra et al. (Acta Ciencia Indica, Chemistry (1985), 11(4), 267-72). The reference teaches the compounds which correspond to the compound of the instant claim when in the instant case  $R^1$  is hydrogen and R is



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phenyl, hydroxyphenyl, nitrophenyl, methoxyphenyl and 3-bromo-2-hydroxyphenyl (see CAS abstract previously provided).

Claim 18 is rejected under 35 U.S.C. 102(b) as being anticipated by Fathy et al. (Journal of Chemical and Engineering Data (1988), 33(2), 218-19). The reference teaches the compound with RN 113111-06-1 which corresponds to the compound of the instant claim when in the instant case R<sup>1</sup> is amino and R is 2-chloro-7-methyl-3-quinoliny (see CAS abstract).

Applicants are advised that copious amount of art is still available but not considered at this time due to the enormous volume. Out of 140 references only references numbered 100-140 have been considered.

***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim 18 is again rejected under 35 U.S.C. 103(a) as being unpatentable over Blum et al. (US 6,107,487). The reference teaches the compound of example 10 (see cols 13-14). The claim differs by having a hydrogen over the prior art methyl on the ring nitrogen of the pyrazolinone. The basis of this rejection is the same as given in the previous office action and is incorporated herein fully by reference. Applicant's argument is not on point. Applicants must prove that their compounds possess a property that the prior art compounds do not possess, not is not disclosed to possess. In re Dillon (16 USPQ 1897) states "the discovery that a claimed composition possesses a property not disclosed for the prior art subject matter does not by itself defeat a prima facie case."

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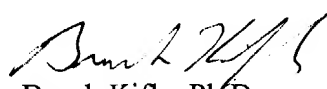
Claim 18 is again rejected under 35 U.S.C. 103(a) as being unpatentable over Mitra et al. (Acta Cienc. Indica, Chem. (1985), 11(4), 267-72). The reference teaches compounds embraced by the generic claim 1 which Applicants have now excluded by proviso. However, compound that are analogues, homologues or ring position isomers of these prior art compounds are embraced by the claim and render the claim obvious. The basis of this rejection is the same as given in the previous office action and is incorporated herein fully by reference. Applicants' arguments that the claims do not have species suggested by the examiner is wrong. The species pointed to are embraced by claim 18.

Applicants are advised of US 6,455,525 that claims similar subject matter.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruck Kifle, Ph.D. whose telephone number is 571-272-0668. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund J. Shah can be reached on 571-272-0674. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

  
Bruck Kifle, Ph.D.  
Primary Examiner  
Art Unit 1624

BK  
April 7, 2004